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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,078	01/21/2004	Klass P. Hardeman	047446/273072	4620

826 7590 05/11/2007

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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
05/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,078	HARDEMAN ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *January 26, 2007 (amendment)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-15 and 17-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 8-15 and 17-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 4/16/2007
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims **5-7 and 16** have been cancelled, claims **1-4, 8 and 19-31** have been amended, the disclosure has not been amended, and no new claims have been added as per the amendment filed January 26, 2007. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of this Office action. The declaration filed under 37 C.F.R. §1.132 by Mssr. S. E. Hall along with three appendices has also been received.

Claims **1-4, 8-15 and 17-31** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1-31** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for a limited number of nucleotides linked though a terminal phosphate group to a solid support and the synthesis thereof, does not reasonably provide enablement for the vast array of compounds, some linked to a solid support and some not linked to a solid support, and the synthesis thereof, encompassed by instant claims **1-30**, and to the method of testing encompassed by claim **31**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The reliance of the independent claims on incompletely defined or non-defined terminology renders the claim vastly over broad in scope.

B. The nature of the invention: The invention is directed to compounds wherein a terminal 5'-nucleotidyl unit with optionally multiple O-P-O linkages is attached to an intermediate linker or linkers and these linkers are ultimately alternatively attached to a solid support, "a tag," or "a protective group." The invention is also directed to methods of making these compounds, and to a method of testing apparently based on affinity chromatography

wherein the above noted compounds, when attached to a solid support, play a key role in the analysis of proteomes; aka mixtures of compounds derived from the internal components of intact cells following disruption.

C. The state of the prior art: Affinity chromatography is well known in the prior art, but presently there is no single reference which discloses all of the details of the instant claimed compounds, their method of making, or their application in affinity chromatography.

D. The level of one of ordinary skill: One of ordinary skill would not find the syntheses or the affinity chromatography methods disclosed herein to be difficult to execute if the compounds being used therefore are as well defined as provided for in the numerous examples found in the disclosure, but would find such exercises much more difficult because of the lack of well defined definitions of the "compound[s]" as presently of record in the claims.

E. The level of predictability in the art: Compounds which structures similar to the prior art affinity chromatography supports are likely to provide results similar to those already established in the prior art. However, this conclusion does not necessarily apply to all of the compounds encompassed by the instant claims.

F. The amount of direction provided by the inventor: The instant disclosure provides a large number of examples of how to make compounds usable in affinity chromatography, but only one prospective description, and no specific embodiments, describing how these compounds might be applied to actual affinity chromatographies.

G. The existence of working examples: As noted above there are many synthetic working examples, but no working examples of how any one of the instant disclosed compounds may be used to carry out affinity chromatography. And also there are no working examples wherein the nucleotidyl moiety is attached to a protecting group or to a "tag."

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be undue because the scope of the compound claims is excessive and because of the total absence of working examples to provide guidance concerning whether the instant compounds actually behave in a predictable manner based on the prior art experience of others with similar affinity chromatographic-capable compounds.

Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive.

Examiner has reviewed the declaration filed by applicant and signed by Mssr. S.E. Hall. Examiner does not doubt that Mssr. Hall and his associates can apply the technology held by, and conveyed to Mssr. Hall applicant, but examiner seriously doubts that one of ordinary skill could reproduce the results provided by the instant declaration because of the meager experimental details provided. For example, the instant declaration together with Appendix A fails to provide the details of what "buffer" or "buffers" are appropriate for the multiple steps briefly summarized in "paragraph 6" and "paragraph 7," and fails to provide any indication of what the cryptic abbreviations are intended to define in the second and the third columns of Table A1. Examiner respectfully suggests amendment of the instant declaration with a much more complete description of how to execute the claimed process and the consequential results thereof. If the method is as readliy applied as asserted, examiner assumes that a more complete and comprehensive disclosure of the details of process execution need not reveal any trade secret information concerning the protein contents of the tested "Jurkat cells."

In addition, the process steps a)-c) of claim **28** are described only with the generic terms "coupling," "end-capping," and "reacting" but without the specific terminology necessary to adequately define the scope of the particular process steps necessary to produce the products embodied herein. A similar criticism continues to apply to the compound claims wherein large areas remain inadequately defined as noted below.

Claims **1, 23-28 and 31** are objected to because of the following informalities:

In claim **1** at line 2, the term "a general formula" is grammatically incorrect. Did applicant intend the term to read -- the general formula --? See also claim **23-27** at line 3 ("a the general structure"), claim **28** at line 2, and claim **31** at line 4 for the same or a very similar error.

Appropriate correction is required.

Applicant's arguments with respect to claims **1, 23-28 and 31** have been considered but are moot in view of the new grounds of objection. This new ground of objection was necessitated by applicant's amendments.

Claims **1-6, 8, 16-28 and 31** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 1, the term "composition" is technically erroneous because said term implies the presence of two or more separate substances; e.g. the term of art "pharmaceutical composition" requires at least one active ingredient and at least one carrier. Examiner suggests that the term -- compound -- should be substituted for the noted term. See also claims **24 and 16-27** wherein the same error is repeated.

Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive.

Examiner notes the dictionary citations provided by applicant wherein the term "compound" and "composition" are defined. The issue appears to concern an intermediate situation wherein the "compound" is "non-homogenous" because of the inherent non-homogeneity of the solid support material. Examiner notes that applicant has admitted that all of the component parts of the substances at issue are chemically linked, but is unwilling to acknowledge that the resultant substance is in fact a compound. Examiner suggests that this debate may be resolved by the substitution of the terms -- non-homogenous compound -- and -- non-homogenous solid support -- or the like in both the claims and the specification, and will not find these substitution to be new matter.

In claim **1** at lines 4-10, the term "substituted" renders the instant claim incompletely defined because the substituents implied thereby have not been defined in the claim. See also claims **28 and 31** wherein similar errors occur.

Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive.

Applicant argues that one of ordinary skill would know the meaning intended by the cited term, but has failed to provide an amendment to the cited claims to address the noted shortcoming. Examiner notes that the disclosure is not the claims and that the prior art guidance quoted by applicant is also not in the claims. Applicant is respectfully requested to provide an amendment to the claims wherein the noted term has been defined.

In claim **1** at line 12, the term "phosphate group mimic" renders the instant claim incompletely defined because the noted term is not further defined in the claim. See also claims **28 and 31** wherein similar errors occur.

Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive.

Applicant argues that one of ordinary skill would know the meaning intended by the cited term, but has failed to provide an amendment to the cited claims to address the noted shortcoming. Examiner notes that the disclosure is not the claims. Applicant is respectfully requested to provide an amendment to the claims wherein the noted term has been defined.

In claim **2** at line 1, the term "further comprises" is incorrect in the instant claim because said term implies that the chemical structure of the compound being claimed contains additional structural component(s) not defined in the claim. Applicant is respectfully requested to substitute narrow language such as -- consisting of-- or the like for the noted term. Examiner suggests that the subject matter of the instant claim may be incorporated into claim **1**, or alternatively, the definition should be amended as the definition of a variant of the generic term "divalent heteroalkyl group." The above noted term also renders the instant claim lacking in proper antecedent basis because claim **1** is now more narrowly defined by the term of art "consisting essentially of." For similar errors see claim **3**

Applicant's arguments with respect to claim **2** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **22** the term "adenosine, ... and uridine" are directed to compounds, not substituents. Appropriate amendment is respectfully requested. See also claims **23-27** wherein a similar error reoccurs. In addition, the term "analog" in claim **22** is indefinite because there is no further definition of what chemical structures are intended to be included within the scope of the claim. Deletion is suggested.

Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive.

Examiner notes applicant's amendments to claims **22-27 and 31** but finds them to be inconsistent and not always correct. Deletion of the terminal letter "e" and replacement thereby with -- yl -- is correct but has not always been entirely accomplished; e.g. see claim **22**. Examiner suggests that a completely accurate correction for each of the names in claims **22-27** would be -- 5-deoxy-5'-adenosinyl -- or the like. And in claim **31** at line 17, the term "nucleoside" should be -- 5'-nucleosidyl --. Appropriate corrections to complete the amendment process are respectfully requested.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **1-4, 8-15 and 17-31** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Trayer et al.** (PTO-892 ref. **R**) in view of **Van Aerschot et al.** (PTO-892 ref. **T**) and further in view of **Shibaev et al.** (PTO-892 ref. **V**).

The instant claims are directed to compounds including a terminal nucleotidyl moiety attached to a solid support by linker(s), to a tag, or to a protecting group, and methods of making same. In addition, the invention is directed to the application of the claimed compounds as adsorbents (aka "mediums") in affinity chromatography.

Trayer et al. discloses the synthesis of numerous adenosine phosphate-type affinity chromatography media and teaches at page 622, column 1 (General Discussion) in addition that the methods disclosed may be used to make analogues of the compounds disclosed.

Trayer et al. does not expressly disclose the particular linker arrangements claimed herein.

Van Aerschot et al. discloses silica adsorbents modified by the attachment of single linkers or combinations of linkers bonded to one another in series for the purpose of attaching a nucleoside or nucleotide unit at the terminus. This reference does not disclose the particular types of solid support derivatized compounds claimed herein.

Shibaev et al. discloses the preparation of affinity chromatographic adsorbents wherein the linkage between the solid support and a nucleotide is a phosphoramidate formed between a solid-support-attached-linker amino group and the terminal phosphate of the nucleotide. **Shibaev et al.** does not specifically disclose the attached nucleotide to be ATP.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made, based on the expansive teachings of **Trayer et al.** to make compounds including the linkers of **Van Aerschot et al.** and the phosphoramidate nucleotide attachment linkage of **Shibaev et al.** to generate compounds reading on the instant claimed subject matter. And one of ordinary skill, again based on the teachings of **Trayer et al.**, would have a reasonable expectation that the resultant compounds would be useful in affinity chromatography.

One having ordinary skill in the art would have been motivated to combine these references because the expansive teachings and examples of **Trayer et al.** motivates the combination with other references to generate alternative structures to those of **Trayer et al.** with similar utility in affinity chromatography.

Therefore, the instant claimed compounds, method of making and method of using would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

Applicant's arguments with respect to claims **1-31** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments wherein the definition of "K" has been narrowed considerably.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to

37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
04/19/2007

4/19/07

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